R. Andrews

This report is required by law (7 USC 2143). Failure to report according to the regulations can result in an order to cease and desist and to be subject to penalties as provided for in Section 2150.

See reverse side for additional information.

Interagency Report Control No 0180-DOA-AN

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

ANNUAL REPORT OF RESEARCH FACILITY
(TYPE OR PRINT)

1. **REGISTRATION NO.** 93-R-0251 **CUSTOMER NO.** 1128

FORM APPROVED
OMB NO. 0579-0036

2. **HEADQUARTERS RESEARCH FACILITY** *(Name and Address, as registered with USDA, include Zip Code)*

AMGEN
ONE AMGEN CENTER DRIVE
THOUSAND OAKS, CA 91320-1789

"A" by K. Dowland 12/15/05 ltr

3. **REPORTING FACILITY** (List all locations where animals were housed or used in actual research, testing, teaching, or experimentation, or held for these purposes. Attach additional sheets if necessary.)

FACILITY LOCATIONS*(sites)*

(b)(2)High, (b)(7)f

REPORT OF ANIMALS USED BY OR UNDER CONTROL OF RESEARCH FACILITY *(Attach additional sheets if necessary or use APHIS FORM 7023A)*

A. Animals Covered By The Animal Welfare Regulations	B. Number of animals being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not yet used for such purposes.	C. Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use of pain-relieving drugs.	D. Number of animals upon which experiments, teaching, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which appropriate anesthetic, analgesic, or tranquilizing drugs were used.	E. Number of animals upon which teaching, experiments, research, surgery or tests were conducted involving accompanying pain or distress to the animals and for which the use of appropriate anesthetic,analgesic, or tranquilizing drugs would have adversely affected the procedures, results, or interpretation of the teaching, research, experiments, surgery, or tests. *(An explanation of the procedures producing pain or distress in these animals and the reasons such drugs were not used must be attached to this report)*	F. TOTAL NO. OF ANIMALS (Cols. C + D + E)
4. Dogs		50	1		51
5. Cats					
6. Guinea Pigs		38	2	86	126
7. Hamsters	6	11	314		325
8. Rabbits	93	90	484	310	884
9. Non-Human Primates					
10. Sheep					
11. Pigs		2			2
12. Other Farm Animals					
13. Other Animals					

ASSURANCE STATEMENTS

1) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anesthetic, analgesic, and tranquilizing drugs, prior to, during, and following actual research, teaching, testing, surgery, or experimentation were followed by this research facility.

2) Each principal investigator has considered alternatives to painful procedures.

3) This facility is adhering to the standards and regulations under the Act, and it has required that exceptions to the standards and regulations be specified and explained by the principal investigator and approved by the Institutional Animal Care and Use Committee (IACUC). **A summary of all the exceptions is attached to this annual report.** In addition to identifying the IACUC-approved exceptions, this summary includes a brief explanation of the exceptions, as well as the species and number of animals affected.

4) The attending veterinarian for this research facility has appropriate authority to ensure the provision of adequate veterinary care and to oversee the adequacy of other aspects of animal care and use.

CERTIFICATION BY HEADQUARTERS RESEARCH FACILITY OFFICIAL
(Chief Executive Officer or Legally Responsible Institutional official)
I certify that the above is true, correct, and complete (7 U.S.C. Section 2143)

SIGNATURE OF C.E.O. OR INSTITUTIONAL OFFICIAL	NAME & TITLE OF C.E.O. OR INSTITUTIONAL OFFICIAL *(Type or Print)*	DATE SIGNED
b6, b7c	b6, b7c	11/22/2005

APHIS FORM 7023 (AUG 91) (Replaces VS FORM 18-23 (Oct 88), which is obsolete

PART 1 - HEADQUARTERS

1. Registration Number: 93-R-0251 / 1128

2/3. Species (common name) & Number of animals used in this study:

Guinea Pigs (86)

4. Explain the procedure producing pain and/or distress.

42 Guinea Pigs: Explain the Procedures Producing Pain and/ or distress:This animal model is a generally accepted model for human multiple sclerosis. An autoimmune mediated encephalomyelitis disease state is created by peripheral immunization containing myelin protein. Animals experience a gradual weakness, rear limb paralysis and weight loss. Although nursing and supportive care is provided to the animals, they may experience distress as a result of the progressive disease state. 44 guinea pigs: Animals were used to screen novel therapeutics for potential activity as a human therapeutic for various respiratory distress disorders, primarily asthma. Experimental protocol resulted in some animals experiencing short-term respiratory distress characterized by airway spasm. Although, bronchoconstriction of this type is not characterized by human asthmatics as a painful experience, it may cause anxiety and distress. Therefore, animals may also experience distress related to this short term, experimentally induced compromise.

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results. (For Federally mandated testing, see Item 6 below)

42 Guinea Pigs: A review of the literature reveals that non-steroidal and/or steroidal agents have anti-inflammatory properties that could affect development and maintenance of the disease model. In addition, narcotic analgesics may cause sedation and/or ataxia and compromise clinical scoring. The inclusion of such compounds would likely affect the very outcomes that are used to determine the effectiveness of tested therapeutic regimens. 44 Guinea Pigs: The bronchoconstriction is distressful to the animals however analgesics would not be expected to actually address this issue with the animals. Broncho-dilatory drugs are also not indicated since they would immediately reverse the experimental bronchoconstriction thereby not allowing the testing of novel therapeutics in reversal of bronchoconstiction. A review of the literature shows that anti-inflammatory analgesics (COX inhibitors, aspirin) may disrupt the production of several eicosanoid species, leading to their anti-inflammatory activity, and these agents have been shown to have profound inhibitory effects on airway inflammation and hyper-reactivity in animal models of asthma which would detrimentally affect the outcomes of drug testing. Anesthetics or tranquilizers are not an option because they have been demonstrated to alter the animals breathing patterns, particularly lowering the respiratory frequency, which can adversely affect the measurements of lung function in the animals with the possibility that we would not be accurately measuring the effects of the novel therapeutics under study. A review of current literature endorses this system of using unrestrained, conscious animals as the most realistic model available to mimic the clinical setting of human asthmatic subjects.

6. What, if any, federal regulations require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g., APHIS, 9 CFR 113.102):

Agency: N/A CFR:

Approval Status:
Approved/Disapproved By:
Date:

Disapproved Reason:

1. Registration Number: 93-R-0251 / 1128

2/3. Species (common name) & Number of animals used in this study:

Rabbits (310)

4. Explain the procedure producing pain and/or distress.

This animal model seeks novel therapies for mitigating pain secondary to inflammatory disease in a species that has high homology with humans for the targeted receptor. An inflammatory response is created, animals are dosed with novel compounds and the analgesic effect tested by scoring limb withdrawal following von Frey stimulation. Animals receiving vehicle controls or ineffective test compounds may experience very short periods of mild pain or distress associated with the induced inflammatory response.

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results. (For Federally mandated testing, see Item 6 below)

Use of analgesics and anti-inflammatory agents will interfere with outcomes observed in this inflammatory pain model. A review of the literature substantiates that anti-inflammatory agents will block the development of inflammation and pain hypersensitivity thereby confounding our ability to assess whether our novel compounds are having a pain-relieving effect. Similarly, the pain-relieving effects of analgesics such as opioids will confound our ability to determine whether our novel compounds are reducing pain. Since our goal is to model inflammatory pain states in humans and identify 1) changes in pain sensitivity and 2) efficacy of novel compounds, analgesics or anti-inflammatory agents cannot be administered.

6. What, if any, federal regulations require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g., APHIS, 9 CFR 113.102):

Agency: N/A CFR:

Approval Status:
Approved/Disapproved By:
Date:

Disapproved Reason: